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ORIGINAL ARTICLES

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THE CLINICAL DIAGNOSIS OF SYPHILIS *

By ERNEST DWIGHT CHIPMAN, M. D., San Francisco

Twenty years ago the dermatologist was often consulted for aid in the diagnosis of syphilis. Today he is called upon with relative infrequency for such service. The reason, of course, lies in the aid afforded by the laboratory in demonstrating the treponema and in the performance of complement fixation tests.

It is by no means the purpose of this paper to belittle the invaluable assistance which the laboratories offer; it is rather to urge that the clinical recognition of syphilitic lesions shall not be allowed to become a lost art.

It will be granted that routine resort to the Wassermann test in all dermatologic cases may bring to light occasional unsuspected positive reactions. It will, likewise, be granted that the occurrence of a positive reaction does not necessarily proclaim a given lesion to be luetic. Still further, it will be generally conceded that, in a certain percentage of

undeniably specific cases, a negative report will be returned.

These facts alone should serve to free us from what Lisser has so aptly termed the tyranny of the Wassermann test.

Without discussing the virtues or the defects of laboratory reports, I believe we may accept two statements:

1. The blood reaction may be conclusive, or it may be of value simply as confirmatory evidence.
2. Clinical signs may be conclusive, or they may be of value simply as confirmatory evidence.

When thus stated, the clinical side of the case seems to balance evenly with that of the laboratory. In the minds of the physicians at large, the tendency has been to exaggerate the importance of laboratory, and to minimize the value of clinical findings.

Now, while we urge that the laboratory be called upon in every case either for original diagnosis or for confirmation, we must urge an equal fidelity to the available clinical signs. And I believe it is especially incumbent upon us as dermatologists to strive to maintain that skill in clinical diagnosis which was the glory of the older school in which many of us were trained and which the easy path to the laboratory may tempt us to neglect.

A few brief case histories will illustrate certain definite points:

Case 1—Mr. S. complained of lesions involving the scalp, forehead, and the flush area of the face. It seemed, obviously enough, a seborrheic dermatitis. With the use of sulphur and salicylic acid the eruption improved, but did not disappear. For several weeks the lesions seemed upon the verge of resolution. At length, there developed a polycyclic arrangement upon the forehead which showed a suspicious degree of infiltration. For the first time, a complete history was taken, and the fact of an initial lesion some twenty years previously was elicited. A blood test was then made with negative result. Nevertheless, all local treatment was suspended, and the lesions promptly vanished under the internal administration of mercury and iodide.

This case illustrates a faulty taking of the history. It illustrates also the neglect of laboratory aid as promptly as might have been useful. Finally, it illustrates the diagnosis through clinical signs after the failure of the laboratory.

Case 2—Mr. B., 57 years of age, had a small patch of leucoplakia on the inner aspect of the lower lip. He gave a history of chancre twenty-five years ago, but had had two years of intensive mercurial medication. Both blood and spinal fluid were reported negative. In spite of these findings, a tentative clinical diagnosis of syphilis was made, and a further

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blood Wassermann was ordered. The return from this test was strongly positive, and under arsphenamin therapy the lesions disappeared.

This case illustrates the fact that a negative Wassermann report is not to cause us to give ground when we are reasonably certain of our clinical signs.

Case 3 is an extreme one—Mrs. P. and her two small daughters all complained of a generalized eruption which was attended with such distressing nocturnal itching that sleep was impossible. The family physician promptly had a blood test performed, and, upon receipt of a negative report, advised the distracted lady that she had nothing to worry about. This illustrates sublime reverence for the laboratory and profound contempt for the acarus.

Case 4—Mrs. N., age 43, divorced, had had a gangrenous condition of the toes for one year. Repeated blood Wassermann tests were uniformly negative. Finally, spinal fluid examination brought a strongly positive report.

Not only this case, but many of the cases we see illustrate the fact that, if we are basing our diagnosis upon laboratory findings, we must often have multiple tests; likewise, if we are basing our diagnosis upon the clinical side, we must study not only the appearance of the lesions, but note their behavior under treatment.

Thompson has described three classes of patients who present themselves for diagnosis: (1) Those with symptoms or lesions which they themselves consider syphilitic; (2) those with symptoms or lesions of which they themselves are doubtful; and (3) those with absolutely no thought of syphilis in their minds.

As in arriving at any diagnosis in general, the time used in the taking of the history is usually well spent. For various reasons, syphilitic patients are prone to lie. Not infrequently they seem bent on testing our skill, and appear satisfied only after the diagnosis is established, in spite of all manner of reticences and evasions. For this reason, the more we can cross-examine without seeming to do so, the quicker the real facts of the case are elicited.

It would be presumptuous to attempt before this section any text-book discussion of the clinical diagnosis of syphilis. But I feel sure that no one will misconstrue a general survey of those clinical signs which have been most helpful in my own practice, particularly as it is certain that in the discussion other useful points will be brought out.

The clinical diagnosis of genital chancre is usually easy, but it is assumed, of course, that the treponema will be demonstrated. Extra-genital chancres are not so easily recognized, because of their unusual and unexpected situations. Occurring upon the tongue or lip, an epithelioma may be suggested. The duration of the lesion and the age of the patient are possible aids. While both may exhibit induration, the epithelioma is capable of a much greater degree of hard border besides which its surface is not so smooth and glistening. It also bleeds much more easily. Occurring upon the cheek, there sometimes develops such extensive edema that the characteristic border of the lesion cannot be recognized. About the finger-nails, the tendency to suppuration may be an obstacle to the diagnosis.

In the secondary stage of syphilis, there are certain general characteristics the recollection of which may be of service.

Of course, the earlier the eruption the more general the distribution. But while the early lesions are more generalized, there are special sites of preference, as the edge of the forehead (*corona veneris*), the angles of the mouth, the nape of the neck, the abdomen, the palms of the hands and, in general, the flexor surfaces.

COLOR

Syphilitic lesions usually present a raw-ham or copper color. This is explained histologically by the infiltration of plasma cells into the corium around the capillaries. If the skin is drawn tensely over the lesions, or pressure applied by a diascop, there remains, after the blood is pressed out, a brownish-yellow stain due to this cellular infiltration. This is quite characteristic.

INDURATION

The same tendency to plasma cell infiltration gives to most syphilides a higher degree of induration than is present in the non-specific lesions with which they might be confused.

CONFIGURATION

Syphilides have certain characteristics of grouping and configuration. They favor serpiginous and gyrate figures, circles and segments of circles, an interrupted circle being most suggestive.

EVOLUTION AND RESOLUTION

There is a wide range in the duration and intensity of the secondary eruption. As a rule, the earlier rashes are more transient and disappear without treatment in a few weeks. The later papular and nodular lesions are more stable, and unless treated may persist over long periods. In resolving, most syphilides leave some degree of stain. This varies somewhat with the complexion, brunettes exhibiting much greater pigmentary changes than blondes. The occurrence of scarring, even though no ulceration has taken place on the surface, is a characteristic of some of the later lesions on resolving. This process of producing scar-tissue in the corium without destroying the overlying epidermis is, according to Wilfrid Fox, practically confined to syphilis and leprosy.

The great general characteristic of the secondary syphilitic rash is polymorphism. The eruption of syphilis may imitate almost any other dermatosis. It may even imitate itself as, for example, a gumma that assumes the appearance of an initial lesion. But the tendency to polymorphism is of service in diagnosis. In conditions such as lichen planus, acne, and psoriasis, a single type of lesion is usually present, while in syphilis one may see at the same time the scaly lesion resembling psoriasis, the shiny papule that suggests lichen and the acne-like pustule.

In a general sense, the character of the cutaneous lesions depends upon the type of skin on which they are found. For example, upon a dry, scaly skin, the eruption will tend to assume a psoriasiform character, while upon an oily skin the syphilides are much more suggestive of seborrheic dermatitis.

Certain cutaneous manifestations are suggestive and some pathognomonic. For example, a fissure at the angle of the mouth is suggestive of lues, although it may be a result of streptococcus invasion; seen in connection with the well-known syph-

ilitic facies, diagnosis is easy. Some of the pigmentary changes are absolutely pathognomonic. One, for example, occurs on the neck, more often in females, and appears as a group of circular depigmented areas. These areas may indicate the spots which were previously faintly discernible macules, but by many they are thought to arise without any antecedent eruption. They are not to be confused with vitiligo, which has a much more map-like contour.

Certain groupings of papules are practically pathognomonic; for example, the corymbose type which indicates a large central papule surrounded by a collection of small satellites. Moist papules, or condylomata, are of exceptional diagnostic interest, as such lesions are seen in no other disease.

MUCOUS MEMBRANES

In the absence of a specific history, especially if concomitant signs are failing, the diagnosis of the lesions of the mucous membranes may offer perplexities. These lesions afford material for comprehensive study all by themselves. At this time, it is well to enumerate some of the possible sources of error. The occurrence of mercurial stomatitis is usually detected because of the knowledge that the drug has been taken, together with the fact that it occurs less frequently on the tongue than the syphilitic erosions. It is seen most often on the gums or cheeks, is more sensitive, and is usually accompanied by signs of salivation and characteristic odor of breath. Aphthous stomatitis is more inflammatory than syphilitic patches, and shows a fine, reddish halo about the lesion.

Erythema multiforme may occur in the buccal cavity without lesions upon the skin. This, too, is painful and inclined to develop vesicles which rupture, and leave superficial ulcerations. Psoriasis, lichen planus and lupus erythematosus, leucoplakia, Vincent's angina, epithelioma, and tuberculosis are all to be considered in the list of possibilities.

Perforation of the hard palate is usually regarded as definitely syphilitic, and indurative atrophy of the tongue is always to be considered in searching for late signs.

SYPHILIS OF THE APPENDAGES OF THE SKIN

Syphilitic alopecia occurs in the secondary stage, and may take the form of diffuse thinning such as occurs after many constitutional infections, or more characteristically, in patches which give the so-called moth-eaten aspect. Loss of hair may occur after destructive lesions have involved the scalp and healed with scar formation. Certain forms of alopecia areata, particularly in young subjects, are possibly the result of congenital syphilis.

NAILS

The diagnosis of syphilitic lesions of the nails is spoken of lightly in text-books as being easy because of the presence of concomitant signs, etc. My personal experience has been the contrary. The diagnosis of indeterminate nail lesions in the absence of specific history has always presented difficulties not encompassed by most writers. Aside from streptococcic infections, the most usual diagnosis is, perhaps, psoriasis. Characteristic evidence of syphilitic infection is the pronounced thickening of the nail at

the distal extremity, the hypertrophic tissue being unduly soft. Varney has described as pathognomonic a concavity of the surface which he calls saucer-shaped nails.

Inasmuch as the complement fixation test is less dependable in the later stages of syphilis, the clinical recognition of the tertiary lesions is of the greatest importance.

The nodular syphiloderm is to be differentiated from epithelioma and tuberculosis. Upon either the skin or the mucous membrane, cases will be found which are difficult for the most astute clinician, however nicely the differentiation may appear in parallel columns on paper.

The evolution of an epithelioma is slower, as a rule; its borders are more everted, and there are glandular enlargements. The age of the patient may also help in a corroborative manner.

In the breaking down of the syphilitic nodule, the tendency to form contiguous arcs of circles is one of the most dependable helps in diagnosis. In contra-distinction to this definite tendency toward regular circular lines in syphilis, the tubercular lesion often manifests a corresponding leaning toward irregular lines and angles. The tubercular lesion is also more painful.

Upon the leg the broken-down nodule may be confused with varicose ulcer and erythema induratum. The grouping of circular ulcers on the upper third of the leg is characteristic of syphilis, while varicose ulcers most often involve the lower portions, are irregular in outline, and are surrounded by pigmented and often eczematous skin. Erythema induratum usually occurs in young women, and the lesions are accompanied by a degree of pain which is disproportionate to their indolent aspect. The diagnosis is sometimes made obscure by the tendency to describe "punched-out" ulcers as characteristic of syphilis. I emphatically repudiate any such sentiment. Erythema induration may present a typical punched-out appearance; so may epithelioma and, sometimes, varicose ulcers.

The scarring which results from the healing of syphilitic nodules is often so characteristic that the diagnosis may be suggested by it. A white center with relatively narrow border of sepia-brown color is strongly indicative of syphilis.

350 Post Street.

DISCUSSION

Thomas J. Clark (Oakland Bank Building, Oakland)—The title of the author's paper, "The Clinical Diagnosis of Syphilis," should arouse all the enthusiasm of the dermatologist in helping to restore to medicine in general the most careful examinations for all skin cases.

The very efficient work of the laboratories today gives a short cut in the syphilitic field that is deadening to the more substantial and enlightening clinical examination.

Dr. Chipman states the case as one of offset or balance as between the laboratory findings and the clinician. That may be very well for keen observers, but where does the laboratory lead us as we get more remote in time from the initial infection? I think he will agree there is much too great reliance given to negative reports in judging the true status of the patient. It would appear that medical men, in examining patients, are confronted with so many situations that may be interpreted variously—they gladly look for a "yes" or "no" answer from the laboratory.

We have to realize that medicine is still an art, employing a very few scientific aids.

The clinical recognition of syphilis involves its differentiation from so many other skin processes, it is the part of wisdom that this protean disease should be classified as a part of dermatology. No one can be better able to recognize syphilitic lesions, all their variations in distribution, configuration, color, and permanent changes after resolution, than the skin man.

It is well to keep one's perspective in looking for syphilis—the start from the initial lesion of slow development, building up of infiltration of closely crowded cells, the gradual diffusion through the lymphatics, to the general system with its widely distributed and symmetrically located lesions, to the gradual recession of the infection, to comparatively narrow localization in the late stages. Then, too, in its inflammatory characteristics syphilis is sluggish, subacute or chronic, and does not easily suppurate. The infiltration with cellular deposit goes on from a central point and progresses outward, leaving a gradually clearing central depression. Syphilis, for a time, builds up tissue on tissue, and this is eventually absorbed and leaves connective fibers to replace the essential parenchyma. This feature of gradual resolution with scarring, and then invading new situations, it is very well to recognize as a cardinal point in diagnosis.

The lack of subjective symptoms is a striking one in most syphilitic lesions. It is often surprising to see extensive lesions in the mouth and throat, and the patient offering very little complaint. The bone pains and headaches of the secondaries are exceptions. At this stage, the patient is often very miserable.

Of course, the experience of the dermatologist precludes his mistaking such diseases as seborrheic dermatitis, pityriasis rosea, psoriasis, alopecia areata, acne vulgaris, lupus vulgaris, erythematous lupus, epitheliomata, and leprosy, but about all of these it is less easy for the physician of limited skin observations to feel content in his mind.

The distortions of development and the bone lesions of hereditary syphilis may be mistaken for tuberculosis.

Howard Morrow (380 Post Street, San Francisco)—Our experiences with clinical laboratories in the matter of dark field examinations have been unsatisfactory. This applies particularly to dark field examinations for *treponema pallidum*. The mode of procuring the serum for examination is very important, and careful and prolonged examinations are frequently necessary; consequently, it is essential for physicians who are handling this type of disease to be equipped and trained for dark field examinations.

The Wassermann reactions are so standardized that the reports from most laboratories are satisfactory. In early lues it is seldom difficult to make a positive clinical diagnosis, so the Wassermann reaction is rarely essential. The one exception to this statement is when spirochetes cannot be demonstrated and the Wassermann reaction becomes positive before the appearance of secondary clinical signs. In such cases, the blood should be examined every few days, as it is important to start abortive treatment as early as possible.

Hiram E. Miller (380 Post Street, San Francisco)—Syphilitic patients that are referred to the dermatologist or syphilologist for aid in diagnosis generally fall into one of the two following groups:

1. Patients with a syphilitic lesion, but with a negative complement fixation test.
2. Patients with a positive complement fixation and a non-syphilitic skin lesion that has not responded to anti-luetic therapy.

Dr. Chipman has very ably brought out the many causes for this. The medical profession, however, is not solely responsible for this state of affairs. A

patient is often unwilling to accept a diagnosis of syphilis when he knows that his blood report is negative.

Unfortunately, most of these syphilitic patients that we see have late syphilis. The early ones, in whom the chances of cure are most ideal, are referred to the laboratory man for consultation. He often is less experienced in dark field examination than the dermatologist, and knows little or nothing of the clinical aspects of the disease. I cannot agree with Dr. Chipman when he states that the clinical diagnosis of genital chancre is easy. The primary lesions that have been cauterized, that have a superimposed dermatitis from medication, or that are associated with a Ducrey or gonorrheal infection, are very frequently met with. The correct diagnosis of such lesions is often most difficult, while an incorrect one may deprive the patient of the early and abortive treatment to which he is entitled.

In the differential diagnosis of syphilis of the nail, Dr. Chipman does not mention ringworm of the nail. I think it is one of the most common and most difficult diseases to differentiate clinically from syphilis of the nail.

Dr. Chipman states that "syphilitic patients are prone to lie." When one considers the intimate nature of the information that we ask them to divulge, I think they are remarkably frank and honest.

J. W. James (Sacramento)—Dr. Chipman's paper brings aptly to the front the oft-discussed question of too much reliance on laboratory methods, and not enough skill in observation. Naturally, in this age of mechanics and applied engineering, our training is along paths of exactness with scientific proofs of theories before they are accepted as facts. We seem entirely surrounded by gauges and measures and all kinds of meters. We would take, with great misgiving, an engineer who gave his opinion of some contemplated engineering work without making computations and giving figures.

In an age when no such methods as we now have existed, medical men depended entirely on close observation, and we are forced to admire the acuteness of some of their keen intellects. Their observations on the eruptions and other manifestations of syphilis have not been greatly improved in our time. They lacked what we lack without the laboratory—a more nearly exact diagnosis. I firmly believe the most beneficial results will result from using the laboratory last as an additional evidence until such a time as laboratory proof is final and always sure. A given case that has a negative Wassermann and yields to mercury and iodides is very presumably syphilis, but we are not sure. How are we to prove that some other disease or some well-known and self-limited disease has been cured or coincidentally relieved under treatment? Chills and fever may dissipate under the administration of quinine, but would we presume to declare that this fact alone is a proof of malaria?

The primary and secondary symptoms are most puzzling, although the hidden gummata of the tertiary are far from simple. Tabes, for example, would still be a dark subject except for exact methods, although keen observation was quite right concerning the cause of this malady before the use of the Wassermann test.

I believe a good method to follow is, after all clinical evidence possible has been sifted, a presumptive diagnosis. Then add the laboratory findings in parallel columns for or against the presumed diagnosis.

As Dr. Chipman has well pointed out, laboratory diagnosis alone is fatal and would, in the long run, prove less valuable than clinical methods alone. In the perfection of both methods, we are slowly traveling toward a more nearly exact science.

Robert B. Hill (Merchants' National Bank Building, Los Angeles)—In the attempt to diagnose syphilis, all possible aid should be employed; the early

lesions, contrary to the views of many, are sometimes quite difficult to classify. As Dr. Miller has said, the demonstration of spirochaetes is many times rendered impossible by cauterization and applications of mercurials. The only safe plan to follow is to avoid using any kind of medication on a genital sore until the presence or absence of spirochaetes can unquestionably be determined; it may mean one dark field examination or it may mean many.

I do not believe that anyone can become so proficient in the diagnosis of skin lesions by clinical observations alone, that he can always be sure whether or not a particular lesion is syphilitic. As evidence, a case recently presented with a rather atypical eruption scattered diffusely over the entire body, the patient had been under the observation of a very prominent dermatologist for six months, and at one time during the period had been quarantined for smallpox for seventeen days. A Wassermann test showed a strongly positive reaction, and the skin lesions promptly disappeared under anti-luetic treatment.

William L. Rich (Boston Building, Salt Lake City, Utah)—Dr. Chipman has very well stressed the important points in the skin manifestation of syphilis. I quite agree with Dr. Miller that the clinical diagnosis of genital chancre is often most difficult, and I also agree with Dr. Chipman that it is now made easy by the dark field examination.

It may be well to add that in cases of treated primary lesion or where a secondary infection prevents one in obtaining suitable material for a dark field examination, puncturing the adjacent lymphatic gland will usually clear up the diagnosis.

As an example, the following case is cited: G. T., age 21, was seen in consultation in August, 1922; had a marked induration and oedema of glans penis, with painful micturition. No primary lesion was visible. The history was suggestive, as well as the induration. The right inguinal gland was punctured, and $\frac{1}{2}$ cc. of normal saline injected. The needle was then rotated at various angles until one was able to draw up a small quantity of slightly blood-stained gland juices which, under dark field examination, revealed many treponema pallidum. Treatment was instituted immediately. At the same time blood was taken for a Wassermann test, which later proved negative. Without the use of further local treatment, the lesion rapidly melted away, and this individual has since had several negative Wassermann tests as well as negative physical signs and symptoms.

I also agree with Dr. Chipman in his discussion of serological diagnosis versus careful history and an examination by a trained eye of clinical manifestations. The latter, of course, being vastly the most important, and the former a valuable aid in many doubtful cases.

Doctor Chipman (closing)—It is gratifying that the simple outline presented should have evoked such valuable discussion. Dr. Miller would seem to dissent in two or three details, but I believe that, in reality, we are in accord.

Dr. Miller thinks the clinical diagnosis of complicated chancres is difficult; so do I. My contention was that the clinical diagnosis is usually easy, an opinion I am bound to retain, since there is nothing much easier in dermatology than the clinical diagnosis of the usual or typical chancre. Dr. Miller is correct in stressing the difficulty of differentiating ringworm and syphilis of the nails by their clinical appearances. I tried to emphasize the difficulty of finger-nail diagnosis in general. Tricophyton infection assuredly belongs in the group concerned.

The essence of the paper is a plea for progress in the clinical recognition of syphilis. It is obvious that both clinical and laboratory aids are needed. Sometimes one suffices, and sometimes the other; oftentimes the two combined are not enough.

ACUTE EPIDEMIC ENCEPHALITIS

By JOHN W. SHUMAN, M. D.

The object of this article is to discuss some points referable to the diagnosis of acute epidemic encephalitis, to briefly report my experience with the disease in Syria (ten cases) during the winter of 1922-1923, and a word concerning its treatment with anti-encephalitic serum.

Acute epidemic encephalitis is one of the three important non-suppurative inflammatory diseases of the central nervous system. The other two are poliomyelitis and syphilis. Poliomyelitis and encephalitis are both really poli-encephalomyelitis, the one chiefly affecting the cord and the other the brain. Little difficulty is experienced in differentiating between the two if the disease is a clear-cut brain or cord lesion, but if it is the medulla oblongata that is involved the diagnosis is then most difficult. If the patient lives—and most do—the flacid paralysis and muscular atrophy will be in favor of poliomyelitis. Poliomyelitis usually occurs in summer, and encephalitis in the winter; but it must be remembered that both may attack in the fall of the year.

Syphilis does not often produce a clinical picture of encephalitis. A connecting point, between the two diseases, however, is the apparent existence in encephalitis of a progressive cerebral disease coming on long after the acute illness and separated from it by a long period of seemingly good health. Especially is this true of the Parkinsonian syndrome. In these late or tertiary cases there is no reason to believe that a new infection from without has taken place. The view now is that the virus, like that of syphilis, may lie dormant for years and then give rise to a more chronic and degenerative process than the one encountered in the primary disease. Another resemblance to syphilis is the Argyle-Robertson or "frozen" pupil.

TEN CASES

From the accompanying chart it can be seen that the greatest number occurred in the winter and early spring months, and that all were young. Seven were lethargic, five had twitchings, six had paralysis of the motor oculi nerve, and small pupils which reacted sluggishly to light. On all that eye ground readings could be secured by Charles Webster, M. D., he found an optic neuritis. A leucocytosis was common, with an increase of the polymorphonuclear cells. Gingivitis was pronounced so early in two of the number that it was thought to be the focus of infection. One had marked herpes labialis. On only one was a spinal puncture made, and that just prior to death. In this disease I feel that the spinal fluid analysis is of such little value, and the puncture sometimes harmful, that it is contraindicated. Eighty per cent of our ten cases recovered, and in them no spinal paracentesis was performed. It is hardly fair to include patient number seven in the mortality list, for his precipitate birth quite likely would have been caused by any febrile disease, and his chances for dying 100 per cent.

Only the two last cases received the anti-encephalitic serum, for we did not receive it until the latter part of March, 1923. It will be interesting to learn if the post-encephalitis effects in these cases will be young, are found frequently as sequelae of the dis-